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Development and validation of a claims-based prediction model for COPD severity☆

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Summary
Background: Administrative claims are an important data source for COPD research but lack a validated measure of patient COPD severity, which is an important determinant of treatment and outcomes.
Methods: Patients with ≥1 diagnosis of COPD and spirometry results from 01/2004-05/2011 were identified from an electronic health records database linked to healthcare claims. Patients were classified into 3 COPD severity groups based on spirometry and Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines: GOLD-Unclassified, Mild/Moderate, and Severe/Very Severe. A multinomial logistic regression model was constructed using claims data from 3 months before and after (observation period) the most recent spirometry (index date) to categorize patient COPD severity. A random selection of 90% of patients in each severity level was selected to build the model, and the remaining 10% were used as a validation sample. Model predictions were evaluated for sensitivity, specificity, accuracy, and concordance.
Results: Among 2028 COPD patients who met sample selection criteria, 886, 683, and 459 patients were in the GOLD-Unclassified, Mild/Moderate, and Severe/Very Severe categories, respectively. The final model included age, sex, comorbidities (such as pulmonary fibrosis and

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; ER, emergency room; EHR, electronic health record; FEV_1, forced expiratory volume for one second; FVC, forced vital capacity; GHP, Geisinger Health Plan; GHS, Geisinger Health System; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICD-9, International Classification of Diseases, Ninth revision.

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diabetes), COPD-related resource utilization (such as oxygen use), and all-cause healthcare utilization. In the validation sample, the model correctly predicted COPD severity for 62.7% of all patients (accuracy for predicting GOLD-Unclassified: 73.5%; Mild/Moderate: 70.6%; Severe/Very Severe: 81.4%) with kappa = 0.41.
Conclusions: The prediction model was developed using clinically measured COPD severity to provide researchers an approach to classify patients using claims data when clinical measures are not available.

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by persistent airflow obstruction to the lungs that is not fully reversible [1]. COPD affects over 24 million American adults [2] and costs approximately $50 billion per year [3]. Given its substantial disease burden, administrative claims are a valuable data source for studying real-world COPD-related economic and health outcomes for large populations, providing rich data on treatment patterns, costs, and healthcare utilization.

For claims analyses, measuring disease severity plays a critical role in accurately characterizing samples, performing statistically valid comparisons, and serving as a study outcome. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines suggest classifying COPD severity based on spirometry — specifically, the forced expiratory volume for one second (FEV_1) and the proportion of the forced vital capacity exhaled in the first second (FEV_1/FVC) [1]. The classification of COPD severity via spirometry is important as it constitutes the basis of treatment recommendations [1] and corresponds to significant differences in health outcomes [4—8]. However, since clinically measured COPD severity is not observable in claims data, claims studies use a wide range of proxies for COPD severity, including comorbidities and evidence of COPD exacerbations [9,10]. Reliance on proxy measures rather than clinical spirometric data to define COPD severity may be less accurate.

The objective of this study is to use clinically measured COPD severity to develop a claims-based method, which can be used to predict patient severity when pulmonary function data is unavailable. A COPD severity measure developed using clinical data and information readily available in claims as predictors may prove useful when examining COPD in future claims analyses.

Materials and methods

Data source

This study used de-identified data from the Geisinger Health System (GHS), an integrated health system in Pennsylvania comprising over 700 multi-specialty physicians, 3 hospitals, 40 ambulatory clinics, and 3 research centers, which also offers insurance coverage through the Geisinger Health Plan (GHP). GHS database has a cumulative patient base of approximately 3 million lives and includes linked EHR and GHP claims data. This study used linked data from January 2004 to May 2011 for patients with GHP insurance, who account for approximately 50% of all patients in the EHR data. Claims data capture both in-network and out-of-network (outside GHS) resource use and include medical, hospital, and pharmacy claims for GHP members. EHR pulmonary function test results from spirometry included actual, predicted (based on patient's age and sex), and percent predicted values (actual/predicted × 100) for FEV_1, FVC, and FEV_1/FVC ratio.

Study design and sample

Patients were retrospectively selected if they had a recorded COPD diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9] codes 491 [chronic bronchitis], 492 [emphysema], or 496 [chronic airway obstruction]) and EHR results from at least one spirometry test.

For each patient, the most recent spirometry result meeting the following criteria was selected. First, tests with claims data available both 3 months prior to and following were selected. The 3-month post-period was included to capture medication use and treatment following a test, which would likely be associated with COPD severity. Second, in this 6-month window, patients were required to have continuous eligibility in GHP to ensure complete resource utilization information, which excluded patients who potentially died during the observation period, and no recorded asthma diagnoses (ICD-9 code 493) to safeguard against potential misdiagnosis of asthma. Third, spirometry within 1 week of a COPD exacerbation were excluded, as GOLD guidelines categorize severity in reference to a patient's baseline severity. Spirometry during an exacerbation may overstate a patient's underlying severity and can be difficult for a sick patient to perform properly, leading to an inaccurate measurement [1]. COPD exacerbations were identified using a modified version of the algorithm developed by Mapel et al. [10] (e-Appendix 1). If multiple tests were eligible, the most recent spirometry test was selected. Alternatively, choosing the test with the most severe reading among all eligible tests was considered but had no effect on the severity distribution. The 6-month window — 3 months before and after the selected spirometry test — was defined as the observation period.

COPD severity

Patients were categorized into 4 COPD severity levels (Mild, Moderate, Severe, Very Severe) based on GOLD guidelines

(e-Appendix 2) [1]. Patients diagnosed with COPD who could not be categorized into one of the GOLD categories ($FEV_1/FVC \geq 0.70$) were defined as "GOLD-Unclassified". This separate category was created because, while severity was unidentified by spirometry, it was important to include all COPD-diagnosed patients with a spirometry reading, as these patients would likely be observed in a typical claims database. "GOLD-Unclassified" patients may include those misdiagnosed with other lung conditions, such as pulmonary fibrosis, or COPD patients unable to complete the test because of obesity, which limits the diaphragm's ability to displace intra-abdominal fat [11]. After classifying patients into these categories, the 5 categories were collapsed into 3 levels — GOLD-Unclassified, Mild/Moderate, and Severe/Very Severe to ensure a reasonable number of patients in each category.

Patient characteristics potentially associated with severity

Patient demographics (e.g., age, gender), medical conditions (e.g., pulmonary vascular disease, osteoporosis), and all-cause and COPD-related healthcare utilization potentially associated with COPD and readily available in claims were selected based on literature review and clinical expert opinion (e-Appendix 3). COPD-related utilization during the 6-month observation period was defined as: an inpatient, emergency room (ER), or outpatient visit with a COPD diagnosis; COPD exacerbation; and COPD medications (e.g., inhaled corticosteroids, short-acting beta-agonists) (e-Appendix 4). COPD-related procedures during the 6-month observation period were also evaluated (e-Appendix 5), including: surgery (e.g., lung volume reduction), pulmonary rehabilitation, and oxygen therapy. These variables were descriptively estimated and compared across the 3 severity levels using pairwise comparisons with the GOLD-Unclassified group.

Model construction

A random selection of 90% of patients in each severity level (training sample) was used to develop the model, and the remaining 10% (validation sample) served to validate the model. Univariable multinomial logistic regressions, with the observed COPD severity level as the dependent variable, were performed on the training sample to assess the association between each potential predictor and COPD severity. Each predictor with $p < 0.50$ for any of the severity categories was included as a potential covariate for the multivariable model.

After the univariable selection of potential predictors, a multivariable multinomial logistic regression model was constructed using the observed COPD severity category as the dependent variable and measures identified in the univariable analysis as potential predictors. Stepwise selection (with threshold $p < 0.50$) was applied to identify the final set of predictors. For each patient, the probability of being assigned into each COPD severity category was predicted using the multivariable model. Each patient was classified in the category with the highest predicted probability.

Predictive performance

For all patients in the validation sample, the patients' predicted and observed COPD severity categories were compared. Sensitivity (e.g., proportion of patients with Severe/Very Severe COPD classified as having Severe/Very Severe COPD by the model), specificity (e.g., proportion of patients without Severe/Very Severe COPD classified as not having Severe/Very Severe COPD by the model), and accuracy (i.e., proportion of patients classified to their true COPD severity categories) were estimated to assess the model's performance. Concordance statistics (Cohen's Kappa) were estimated to evaluate the agreement between predicted and observed categories. Performance of the model was similarly assessed for the training sample.

All analyses were performed in SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results

Patient characteristics

Among patients with a recorded COPD diagnosis and available EHR data, 2028 patients met all the selection criteria

Table 1 Sample selection of chronic obstructive pulmonary disease patients with FEV_1 (actual) spirometry.

Step	Description	Number of patients
1	Patients with at least one diagnosis of COPD in the claims history[a] and available EHR data	29,373
2	Patients with at least one FEV_1 (actual) measure	4138
3	Patients continuously enrolled in Geisinger Health Plan (GHP) during the observation period[b]	3089
4	Patients with no history of asthma during these periods[c]	2428
5	Patients with at least one spirometry test not taken within 1 week of a COPD exacerbation or COPD-related antibiotic or steroid use[d]	2028

COPD = chronic obstructive pulmonary disease; EHR = electronic health record; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; ICD-9 = International Classification of Diseases, 9th revision, Clinical Modification.

[a] COPD was defined by the ICD-9 codes of 491, 492, and 496.

[b] The observation period consisted of the 90 days prior to and the 90 days following the test.

[c] Asthma was defined by the ICD-9-CM code of 493.

[d] Refer to e-Appendix 1 for the algorithm to identify COPD exacerbations and/or COPD-related antibiotic or steroid use, adapted from Ref. [1].

and were included in the final sample (Table 1). Out of the 2028 patients, 886 were categorized as GOLD-Unclassified, 683 as Mild/Moderate, and 459 as Severe/Very Severe. A total of 1824 patients were randomly selected for the training sample, leaving 204 patients in the validation sample. Based on a descriptive assessment of patient characteristics, compared to the GOLD-Unclassified category, the Mild/Moderate and Severe/Very Severe categories had a higher proportion of male patients, higher average age, and more COPD-related resource use (Tables 2–4). More evidence of obesity and pulmonary fibrosis was observed for GOLD-Unclassified patients than those with a known level of COPD severity, which is consistent with previous literature [11].

Prediction model

The final prediction model included demographics, medical conditions, COPD-related resource utilization, and all-cause healthcare visits as predictors of three COPD severity categories (Table 5). More severe COPD was positively associated with being male and older. Osteoporosis was positively associated with COPD severity; whereas, pulmonary fibrosis, skeletal muscle dysfunction, and obesity were negatively associated with COPD severity. COPD-related ER, inpatient, and outpatient visits and oxygen therapy were positively associated with COPD severity. Other potential predictors of COPD severity, such as respiratory infection, pulmonary vascular disease, and pneumonia, did not demonstrate an association (i.e., did not have a p-value <0.50) so they were not included in the final model.

In the validation sample, the model correctly predicted COPD severity for 62.7% of all patients (kappa = 0.41), with sensitivity of 77.5%, 52.2%, and 50.0% for GOLD-Unclassified, Mild/Moderate, and Severe/Very Severe patients, respectively. Corresponding specificities of the model were 70.4%, 80.0%, and 90.5%, suggesting that the model is highly specific for the Severe/Very Severe category and fairly specific for the Mild/Moderate category. The accuracies were 73.5%, 70.6%, and 81.4% for the GOLD-Unclassified, Mild/Moderate, and Severe/Very Severe patients, respectively, demonstrating fairly high accuracy for all 3 categories. Positive predictive values (PPVs) for the three categories were 67.0%, 57.1% and 60.4% and negative predictive values (NPVs) for the three categories were 80.1%, 76.6% and 86.2%, respectively. Predictive performance for the training sample demonstrated similar results (Table 6).

Discussion

This study used linked claims and EHR data to develop and validate a claims-based algorithm to predict COPD severity. The validated, claims-based severity categories enable researchers using claims data to predict COPD severity in the absence of clinical measures. The algorithm was built using a sample of patients at GHS, a primarily rural, tertiary care center.

The predictive performance of the model suggests that the selected variables provide a reasonable way to differentiate patient severity in future claims analyses. Approximately 63% of patients were correctly categorized by the prediction model. In a null model, with patients randomly classified into one of 3 categories, approximately 33% would be correctly categorized, with sensitivities of 33%, specificities of 67%, and accuracies between 52% and 59%. The proposed model performs better than the null model for patients in all categories and particularly for Severe/Very Severe COPD (specificity of 90.5%). In other words, when applying the prediction model to select Severe/Very Severe patients from a claims dataset, patient categorization is fairly reliable. Moreover, the high sensitivity of the model in predicting patients in the GOLD-Unclassified category (77.5%) shows that the model performs well in correctly identifying these difficult-to-classify patients.

Administrative claims databases are an important source of real-world population-based data for epidemiological, health economics, and outcomes research. Claims data offer a way to assess mortality rates for different COPD populations as well as provide healthcare utilization and cost data to study its economic burden. However, COPD severity information is often needed to accurately characterize study populations. For example, if not adequately taken into account, disease severity may confound comparisons of costs or COPD exacerbation rates across two treatment groups.

Claims-based prediction models are often used to predict disease severity in other diseases such as breast cancer [12], lung cancer [13], and asthma [14]. These studies found similar levels of performance for their prediction models. The current study provides a prediction model that can be used on typical claims data to estimate patients' COPD severity with reasonable accuracy, thus ensuring access to this crucial variable.

Previous severity algorithms have been constructed for use with clinical or survey data and cannot be directly applied to a claims dataset. In a recent study, Goossens et al. [15] developed an algorithm for COPD severity based on data available from a large respiratory clinical trial of moderate to severe COPD patients. The model was built using observed GOLD severity for all patients, who all had a classifiable COPD severity level. The predictors in this model included demographics (age, sex), body mass index (BMI), smoking history, COPD-related therapies, osteoporosis, and hospital admission in the previous year. Although our study shares several similarities, the Goossens et al. model's performance was worse than our model (unweighted kappa = 0.151 vs. 0.41). It should be noted that, unlike our model, the Goosens et al. model cannot be applied to a typical claims dataset because clinical indicators such as BMI and smoking history are not available in claims. Further, some patients diagnosed with COPD will not have classifiable COPD severity (GOLD-Unclassified); however, the Goosens et al. model does not address this population. Our current model included the GOLD-Unclassified category, thus providing an effective method to identify this patient group in claims. Other survey-based studies have developed similar tools to determine COPD severity using clinical and patient-reported measures not usually available in claims data [16–19]. The prediction model reported here attempts to provide a potential

Table 2 Patient characteristics potentially associated with disease severity (demographics, comorbidities, therapies, and exacerbations).[a]

	Observed COPD severity category		
	GOLD-Unclassified $N = 886$	Mild/Moderate $N = 683$	Severe/Very Severe $N = 459$
Demographics			
Age on index date,[b] mean (SD)	67.4 (12.5)	69.9 (11.2)*	70.0 (10.0)*
Male, *N* (%)	463 (52.3%)	447 (65.4%)*	297 (64.7%)*
Spirometry test results			
FEV_1 predicted	79.2 (18.4)	69.0 (14.1)*	36.2 (9.3)*
FEV_1/FVC	78.5 (5.7)	61.5 (6.6)*	46.9 (11.7)*
Comorbidities, N (%)			
Respiratory related			
Respiratory infection	223 (25.2%)	156 (22.8%)	136 (29.6%)
Respiratory distress	366 (41.3%)	195 (28.6%)*	140 (30.5%)*
Pulmonary vascular disease	135 (15.2%)	74 (10.8%)*	62 (13.5%)
Pulmonary fibrosis	101 (11.4%)	37 (5.4%)*	18 (3.9%)*
Acute respiratory failure	28 (3.2%)	5 (0.7%)*	23 (5.0%)
Asphyxia and respiratory arrest	101 (11.4%)	50 (7.3%)*	80 (17.4%)*
Pneumonia	94 (10.6%)	70 (10.2%)	75 (16.3%)*
Lung cancer	53 (6.0%)	58 (8.5%)	32 (7.0%)
Thoracic malignancies	56 (6.3%)	60 (8.8%)	33 (7.2%)
Cardiovascular related			
Hypertension	547 (61.7%)	400 (58.6%)	279 (60.8%)
Heart failure	196 (22.1%)	130 (19.0%)	112 (24.4%)
Ischemic heart disease	345 (38.9%)	268 (39.2%)	169 (36.8%)
Cerebrovascular accident	159 (17.9%)	117 (17.1%)	58 (12.6%)*
Angina	75 (8.5%)	50 (7.3%)	14 (3.1%)*
Other COPD comorbidities			
Diabetes	269 (30.4%)	141 (20.6%)*	117 (25.5%)
Weight loss	28 (3.2%)	18 (2.6%)	17 (3.7%)
Nutritional abnormalities	46 (5.2%)	25 (3.7%)	25 (5.4%)
Skeletal muscle dysfunction	91 (10.3%)	58 (8.5%)	24 (5.2%)*
Osteoporosis	108 (12.2%)	83 (12.2%)	82 (17.9%)*
Bone fractures	31 (3.5%)	26 (3.8%)	14 (3.1%)
Depression	130 (14.7%)	69 (10.1%)*	58 (12.6%)
Anemia	194 (21.9%)	136 (19.9%)	90 (19.6%)
Glaucoma	84 (9.5%)	43 (6.3%)*	37 (8.1%)
Acute renal failure	43 (4.9%)	29 (4.2%)	12 (2.6%)*
Chronic renal failure	105 (11.9%)	101 (14.8%)	54 (11.8%)
Obesity and its comorbidities			
Obesity	114 (12.9%)	37 (5.4%)*	46 (10.0%)
Cholelithiasis (gallstones)	37 (4.2%)	20 (2.9%)	8 (1.7%)*
Osteoarthritis	200 (22.6%)	116 (17.0%)*	61 (13.3%)*
Low back pain	67 (7.6%)	45 (6.6%)	16 (3.5%)*
Gastroesophageal reflux disease	194 (21.9%)	124 (18.2%)	80 (17.4%)
Obstructive sleep apnea	92 (10.4%)	41 (6.0%)*	35 (7.6%)
Pulmonary embolism	34 (3.8%)	13 (1.9%)*	14 (3.1%)
Non-alcoholic fatty liver disease	16 (1.8%)	4 (0.6%)*	8 (1.7%)
Procedures and therapies			
Patients with at least one procedure/therapy, *N* (%)			
Lung volume reduction surgery	26 (2.9%)	17 (2.5%)	7 (1.5%)
Pulmonary rehabilitation	1 (0.1%)	4 (0.6%)	8 (1.7%)*
Oxygen therapy	158 (17.8%)	117 (17.1%)	224 (48.8%)*
Ventilation	76 (8.6%)	34 (5.0%)*	28 (6.1%)
Number of procedures/therapies, mean (SD)			
Lung volume reduction surgery	0.0 (0.2)	0.0 (0.2)	0.0 (0.2)
Pulmonary rehabilitation	0.0 (0.2)	0.1 (0.9)	0.2 (1.8)*
Oxygen therapy	1.4 (3.4)	1.4 (3.5)	4.6 (5.4)*

Table 2 (*continued*)

	Observed COPD severity category		
	GOLD-Unclassified $N = 886$	Mild/Moderate $N = 683$	Severe/Very Severe $N = 459$
Ventilation	0.5 (1.8)	0.3 (1.4)*	0.3 (1.6)
Exacerbation of COPD[c]			
Patients with at least one episode, *N* (%)	218 (24.6%)	182 (26.6%)	161 (35.1%)*
Number of episodes, mean (SD)	0.3 (0.6)	0.4 (0.7)	0.5 (0.8)*

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICD-9 = International Classification of Diseases, 9th revision, Clinical Modification; SD = standard deviation.

[a] Chi-square test or Fisher's exact test if any expected cell count was less than five was used to compare categorical variables. Wilcoxon rank-sum test was used to compare continuous variables. All *p*-values were based on the pairwise comparison to the "GOLD-Unclassified" group. *p*-values less than 0.05 were marked with asterisks.

[b] Index date was defined as the date of the spirometry test.

[c] COPD exacerbation was defined as any of the following events in the observation period: an inpatient hospital stay or an emergency room visit associated with a primary diagnosis of COPD (first-position ICD-9 codes 491, 492, 496); or an outpatient visit with any of the following ICD-9 codes in the first position: 136.3, 466—466.19, 480—486, 487.0, 490, 491.21, 491.22, 494.1, 506.0—506.3, 507, 511.0—511.1, 512, 517.1, 518.0, 518.81, 518.82 and 518.84. Adapted from: Mapel et al.[10]

solution in cases where such clinical measures are not readily available.

Other studies have developed COPD severity scores in the absence of lung function data; however, none have been validated against clinical measures [10,20—26]. For example, Wu et al. [9] developed a severity score based on measures available in claims data using principal components analysis, but their proxy score has not been validated against clinical measures of COPD severity. Mapel et al. classified COPD complexity using comorbid respiratory conditions and medical procedures [10]. In the current study, spirometry results linked to claims data allows for the assessment of the claims-based prediction model using a clinical measure of COPD severity.

Limitations

First, the model was constructed using patients with spirometry reported in the EHR; however, patients with

Table 3 Patient characteristics potentially associated with disease severity (healthcare utilization).[a]

	Observed COPD severity category		
	GOLD-Unclassified $N = 886$	Mild/Moderate $N = 683$	Severe/Very Severe $N = 459$
Healthcare utilization			
Patients with at least one visit, *N* (%)			
Outpatient	885 (99.9%)	682 (99.9%)	459 (100.0%)
ER	226 (25.5%)	138 (20.2%)*	120 (26.1%)
Inpatient	213 (24.0%)	134 (19.6%)*	110 (24.0%)
COPD-related outpatient[b]	19 (2.1%)	23 (3.4%)	53 (11.5%)*
COPD-related ER[b]	398 (44.9%)	468 (68.5%)*	392 (85.4%)*
COPD-related inpatient[b]	23 (2.6%)	25 (3.7%)	39 (8.5%)*
Number of visits, mean (SD)			
Outpatient	13.8 (9.0)	12.3 (8.5)*	12.0 (8.0)*
ER	0.4 (0.7)	0.3 (0.8)*	0.4 (0.7)
Inpatient	0.3 (0.7)	0.2 (0.6)*	0.3 (0.6)
COPD-related outpatient[b]	0.8 (1.2)	1.5 (1.7)*	2.8 (2.4)*
COPD-related ER[b]	0.0 (0.2)	0.0 (0.3)	0.1 (0.5)*
COPD-related inpatient[b]	0.0 (0.2)	0.0 (0.2)	0.1 (0.4)*

COPD = chronic obstructive pulmonary disease; ER = emergency room; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICD-9 = International Classification of Diseases, 9th revision, Clinical Modification; SD = standard deviation.

[a] Chi-square test or Fisher's exact test if any expected cell count was less than five was used to compare categorical variables. Wilcoxon rank-sum test was used to compare continuous variables. All *p*-values were based on the pairwise comparison to the "GOLD-Unclassified" group. *p*-values less than 0.05 were marked with asterisks.

[b] COPD-related outpatient visit, ER visit, and inpatient hospitalization was defined as an outpatient visit, an ER visit, or an inpatient hospital stay, respectively, associated with a primary diagnosis of COPD (first-position ICD-9 codes 491, 492, 496).

Table 4 Patient characteristics potentially associated with disease severity (percent of patients with medications).[a]

	Observed COPD severity category		
	GOLD-Unclassified $N = 886$	Mild/Moderate $N = 683$	Severe/Very Severe $N = 459$
Medications			
Patients with at least one drug claim, *N* (%)			
Any of the following drugs	355 (40.1%)	345 (50.5%)*	306 (66.7%)*
β_2-agonists			
Short-acting			
Levalbuterol	4 (0.5%)	1 (0.1%)	9 (2.0%)*
Salbutamol	147 (16.6%)	157 (23.0%)*	167 (36.4%)*
Long-acting			
Formoterol	1 (0.1%)	5 (0.7%)	7 (1.5%)*
Arformoterol	1 (0.1%)	1 (0.1%)	2 (0.4%)
Salmeterol	17 (1.9%)	24 (3.5%)	36 (7.8%)*
Anticholinergics			
Short-acting			
Ipratropium bromide	41 (4.6%)	34 (5.0%)	59 (12.9%)*
Long-acting			
Tiotropium	84 (9.5%)	135 (19.8%)*	158 (34.4%)*
Combination short-acting β_2-agonists plus anticholinergic in one inhaler			
Salbutamol/ipratropium	66 (7.4%)	81 (11.9%)*	84 (18.3%)*
Methylxanthines			
Theophylline	0 (0.0%)	5 (0.7%)*	14 (3.1%)*
Inhaled glucocorticosteroids			
Beclomethasone	0 (0.0%)	1 (0.1%)	1 (0.2%)
Budesonide	11 (1.2%)	12 (1.8%)	14 (3.1%)*
Fluticasone propionate	35 (4.0%)	43 (6.3%)*	47 (10.2%)*
Combination long-acting β_2-agonists plus glucocorticosteroids in one inhaler			
Formoterol/budesonide	10 (1.1%)	12 (1.8%)	14 (3.1%)*
Salmeterol/fluticasone propionate	69 (7.8%)	101 (14.8%)*	113 (24.6%)*
Systemic glucocorticosteroids			
Prednisone	121 (13.7%)	106 (15.5%)	112 (24.4%)*
Methylprednisolone	12 (1.4%)	10 (1.5%)	8 (1.7%)

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

[a] Wilcoxon rank-sum test was used to compare continuous variables. All *p*-values were based on the pairwise comparison to the "GOLD-Unclassified" group. *p*-values less than 0.05 were marked with asterisks.

spirometry may be different than those without, potentially limiting the usefulness of this model for a wider population. Thus, this prediction model is best applied in claims analyses focusing on patients with spirometry. In this study, approximately 14% of COPD patients with EHR data had spirometry, but this is not a limitation of the EHR data, as 88.3% of all patients with spirometry tests recorded in their claims data have corresponding EHR results available. While spirometry is recommended to clinically diagnose COPD, a study by Han et al. [27] also found low spirometry use — less than one-third of newly diagnosed patients had spirometry — and its use for newly diagnosed COPD decreased with age. This study is also subject to the quality of the spirometry tests, which can sometimes be inaccurate [28].

Second, although asthma is a potential comorbidity associated with COPD, patients with asthma diagnoses were excluded from the study sample to reduce the potential of misdiagnosis. A number of respiratory disease studies suggest excluding patients with overlapping diagnoses (both asthma and COPD) when one of these two diseases are being studied [15,29] because clinicians might face confusion as to how and if they should differentiate these two diseases [30]. A recent study by Hardin et al. suggests that patients with both COPD and asthma may incur more frequent exacerbations compared to patients with COPD only; however, they found that the presence of asthma was not associated with a significant difference in lung function [31]. This selection criterion eliminated 566 patients (approximately 22%) from the final sample. It is likely that some of the measures selected for the final model would change if these patients had been included, and our model may not be applicable to COPD patients with comorbid asthma. Third, this study used specific ICD-9 codes to identify COPD and its associated conditions, which may differ from those used in future studies. For example, we did not use the ICD-9 code 490 to define COPD. This code is often viewed as lacking specificity for COPD, which increases the potential for misclassification [32,33].

Table 5 Results of the multinomial logit regression on COPD severity.

Explanatory variables	Mild/Moderate[a]		Severe/Very Severe[a]	
	Odds ratio	95% CI[b]	Odds ratio	95% CI[b]
Demographics				
Age on index date (continuous)	1.02	(1.01, 1.03)*	1.02	(1.01, 1.03)*
Male (categorical)	1.89	(1.50, 2.39)*	2.38	(1.76, 3.22)*
Comorbidities				
Respiratory distress (categorical)	0.67	(0.53, 0.84)*	0.65	(0.48, 0.87)*
Pulmonary fibrosis (categorical)	0.40	(0.26, 0.62)*	0.14	(0.07, 0.27)*
Acute respiratory failure (categorical)	0.38	(0.14, 1.06)	2.08	(0.91, 4.75)
Asphyxia and respiratory arrest (categorical)	0.76	(0.49, 1.18)	0.74	(0.46, 1.17)
Lung cancer/Thoracic malignancies (categorical)	1.61	(0.99, 2.63)	1.55	(0.83, 2.88)
Cerebrovascular accident (categorical)	1.05	(0.78, 1.43)	0.73	(0.49, 1.10)
Angina (categorical)	0.94	(0.62, 1.43)	0.28	(0.14, 0.57)*
Nutritional abnormalities (categorical)	1.00	(0.58, 1.73)	1.91	(1.00, 3.65)*
Skeletal muscle dysfunction (categorical)	0.93	(0.63, 1.37)	0.40	(0.23, 0.69)*
Osteoporosis (categorical)	1.35	(0.95, 1.91)	2.04	(1.35, 3.09)*
Bone fractures (categorical)	1.46	(0.80, 2.67)	0.68	(0.30, 1.53)
Glaucoma (categorical)	0.64	(0.42, 0.97)*	1.06	(0.65, 1.73)
Renal failure (categorical)	1.56	(1.12, 2.19)*	0.93	(0.60, 1.44)
Diabetes (categorical)	0.55	(0.42, 0.72)*	0.67	(0.49, 0.93)*
Obesity-related condition (categorical)[c]	0.66	(0.52, 0.82)*	0.48	(0.36, 0.64)*
COPD exacerbation (categorical)	1.20	(0.90, 1.60)	0.95	(0.66, 1.38)
Procedures and therapies				
Lung volume reduction surgery (categorical)	0.85	(0.39, 1.87)	0.32	(0.10, 1.00)*
Oxygen therapy (categorical)	1.08	(0.77, 1.52)	4.51	(3.17, 6.41)*
Ventilation (categorical)	0.78	(0.49, 1.24)	0.72	(0.41, 1.27)
Medications[d]				
Short-acting β_2-agonist (categorical)	1.16	(0.86, 1.56)	1.68	(1.20, 2.36)*
Long-acting β_2-agonist (categorical)	1.32	(0.67, 2.58)	2.09	(1.04, 4.20)*
Short-acting anticholinergics (categorical)	0.84	(0.50, 1.42)	1.48	(0.87, 2.52)
Long-acting anticholinergics (categorical)	1.64	(1.16, 2.33)*	2.32	(1.58, 3.41)*
Combination short-acting β_2-agonist plus anticholinergic in one inhaler (categorical)	1.35	(0.93, 1.97)	1.88	(1.24, 2.86)*
Inhaled glucocorticosteroids (categorical)	1.17	(0.72, 1.89)	0.78	(0.45, 1.35)
Combination long-acting β_2-agonist plus glucocorticosteroids (categorical)	1.52	(1.06, 2.18)*	1.69	(1.14, 2.52)*
Utilization variables				
All-cause ER visit (categorical)	0.88	(0.66, 1.18)	1.26	(0.87, 1.84)
All-cause inpatient visit (categorical)	0.99	(0.72, 1.36)	1.50	(1.00, 2.25)
Number of all-cause outpatient visits (continuous)	0.98	(0.97, 1.00)*	0.97	(0.96, 0.99)*
COPD-related ER visit (categorical)	1.46	(0.70, 3.04)	2.99	(1.41, 6.35)*
COPD-related inpatient visit (categorical)	1.29	(0.64, 2.61)	1.79	(0.84, 3.82)
COPD-related outpatient visit (categorical)	1.82	(1.44, 2.31)*	3.18	(2.28, 4.44)*

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ER = emergency room; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICD-9 = International Classification of Diseases, 9th revision, Clinical Modification.

[a] The GOLD-Unclassified group was the reference category.

[b] *p*-values less than 0.05 are marked with asterisks.

[c] Obesity-related conditions were defined as ICD-9 codes for the following conditions: obesity, cholelithiasis (gallstones), osteoarthritis, low back pain, gastroesophageal reflux disease, obstructive sleep apnea, pulmonary embolism, and non-alcoholic fatty liver disease.

[d] Short-acting β_2-agonist = levalbuterol, salbutamol; Long-acting β_2-agonist = formoterol, arformoterol, salmeterol; Short-acting anticholinergics = ipratropium bromide; Long-acting anticholinergics = tiotropium; Combination short-acting β_2-agonist plus anticholinergic in one inhaler = salbutamol/ipratropium; Inhaled glucocorticosteroids = beclomethasone, budesonide, fluticasone propionate; Combination long-acting β_2-agonist plus glucocorticosteroids = formoterol/budesonide, salmeterol/fluticasone propionate; Systemic glucocorticosteroids = prednisone, methylprednisolone.

Table 6 Evaluation of the multinomial logit prediction model of COPD severity.

	Observed COPD severity category				
	GOLD-Unclassified	Mild/Moderate	Severe/Very Severe		
Training sample ($N = 1824$)					
Predicted COPD severity category					
GOLD-Unclassified	75.4%	43.2%	22.3%	Correctly predicted	59.2%
Mild/Moderate	18.6%	44.3%	27.6%	Kappa	0.35
Severe/Very Severe	6.0%	12.5%	50.1%		
Sensitivity	75.4%	44.3%	50.1%		
Specificity	65.2%	78.3%	91.1%		
Accuracy	69.7%	66.9%	81.9%		
Validation sample ($N = 204$)					
Predicted COPD severity category					
GOLD-Unclassified	77.5%	33.3%	23.9%	Correctly predicted	62.7%
Mild/Moderate	16.9%	52.2%	26.1%	Kappa	0.41
Severe/Very Severe	5.6%	14.5%	50.0%		
Sensitivity	77.5%	52.2%	50.0%		
Specificity	70.4%	80.0%	90.5%		
Accuracy	73.5%	70.6%	81.4%		

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.

While this analysis involved a large database in which all claims were captured, this study involves limitations of all claims analyses, such as potential coding inaccuracies and incomplete claims. COPD treatments may also change over time. To mitigate this issue, we incorporated drugs into our model at the class level. As new classes of COPD treatments become available, our model would need to be updated to incorporate these new drug classes. Further, we used the GOLD classification of COPD severity available at the time of the analysis to define severity. The most recent GOLD severity definition also incorporates exacerbations, the Modified Medical Research Council questionnaire (mMRC) score for breathlessness, and the COPD Assessment Test (CAT) score. While we did include COPD exacerbation as a severity predictor, due to data limitations, we did not use the new COPD severity definition, and developing a claims-based prediction algorithm aligned with this new definition is a subject for future study. Lastly, further study is needed to assess the generalizability of this model to other patient populations.

Conclusions

In this analysis, a COPD severity prediction model was developed using spirometry and predictors typically available in claims data. The relevant predictors identified included demographics, medical conditions, COPD-related resource utilization, and all-cause healthcare visits. Using claims data provides reliable information regarding health utilization and comorbidities and provides a better prediction model for use in future claims-based analyses.

Conflicts of interest

Dr. Macaulay, Ms. Sorg, Ms. Yan, Dr. De and Dr. Wu are employees of Analysis Group, Inc., which received consulting fees from Forest Research Institute for this research. Dr. Sun is an employee of Forest Research Institute. Dr. Simonelli is an employee of Geisinger Health System and received consulting fees from Forest Research Institute for this research.

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Author contribution

All of the authors meet the requirements for authorship and have made substantial contributions to the conception, design, acquisition of data, analysis, or interpretation of data and drafting and revising of the article. All authors approved the final version of the manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmed.2013.05.012.

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